REMARKS

Claims 44, 45, 47, and 55-59 are pending in the application. No amendments have been made by the present response.

35 U.S.C. §112, First Paragraph (Enablement)

At pages 2-3 of the Office Action, claims 45, 47, 55, 56, 58, and 59 were finally rejected as allegedly not enabled. According to the Office Action,

> the specification, while being enabling for a method of treating inflammatory bowel disease with KIM-1-Ig fusion protein, does not reasonably provide enablement for a method of treating an autoimmune disease/immunological disorder in a subject comprising administering an antagonist antibody or antigen-binding fragment thereof that binds to KIM-1, wherein the immunological disorder/disease is inflammatory bowel disease…

Applicant respectfully traverses the rejection in view of the following remarks.

Independent claim 45 is directed to a method of treating an immunological disorder in a subject, the method comprising administering to the subject an effective amount of a composition comprising an antagonist antibody or antigen-binding fragment thereof that binds to KIM-1, wherein the immunological disorder is arthritis or an inflammatory bowel disease. Claims 47, 55, 56, 58, and 59 depend directly or indirectly from claim 45. It is applicant's understanding that examination of the claims has been limited to treatment of an inflammatory bowel disease (i.e., the elected species of "immunological disorder").

As detailed in the response to the first Office Action, the inventor of the present application has discovered that KIM-1 antagonists interfere with T cell activation, suppress IgG response to antigen, and are therapeutically effective in a mouse model of inflammatory bowel disease. In view of these experimental findings, the person of ordinary skill in the art would have reasonably expected antagonist anti-KIM-1 antibodies to be effective in the treatment of inflammatory bowel diseases and the other immunological disorders recited in the claims. Applicant respectfully contests the present Office Action's assertion (at page 2) that "[t]he specification does not provide any evidence that KIM-1 antagonist antibodies would function to [treat] IBD such as ulcerative colitis, ileitis or Crohn's disease" (emphasis added).

The dextran sulfate sodium (DSS) model of inflammatory bowel disease described in Example 12 of the present application is an art-accepted *in vivo* animal model system for inflammatory bowel disease. An *in vivo* animal model example described in the specification constitutes a "working example" if that example correlates with the claimed invention. MPEP § 2164.02. "[I]f the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate." *Id.* Because of the art acceptance of the DSS mouse model for inflammatory bowel disease, the specification (i.e., Example 12) contains a working example indicating that a KIM-1-Ig fusion protein can be used effectively in the treatment of inflammatory bowel disease. Although the working example describes the use of a polypeptide containing the extracellular domain of the KIM-1 protein, whereas the claimed methods are directed to the use of an anti-KIM-1 antagonist antibody, the person of ordinary skill in the art having read applicant's experimental findings would have understood that *any* means of blocking KIM-1 function would be an effective means of treating an inflammatory bowel disease. As is described in the application and as is common in the field of immunology, KIM-1 blockade could be accomplished without undue experimentation either by administration of a soluble KIM-1 protein (as exemplified in Examples 11 and 12, respectively, in an *in vitro* mixed lymphocyte reaction and an *in vivo* animal model of inflammatory bowel disease) or by administration of an anti-KIM-1 antagonist antibody (as exemplified in Example 11 in an *in vitro* mixed lymphocyte reaction). Applicant respectfully submits that the person of ordinary skill in the art would have reasonably expected that inhibition of the KIM-1 signaling pathway via administration of an anti-KIM-1 antagonist antibody to be (like administration of a soluble KIM-1 protein, described in Example 12) an effective means for treatment of an inflammatory bowel disease.

The majority of the present Office Action does not address the specification's disclosure of an *in vivo* working example of treatment of inflammatory bowel disease. Instead, most of the rejection relates to the Office Action's assertion (at page 3) that "the MLC assay, which is art recognized for determining histocompatibility, does not appear to be predictive of general immune responses or treatment of IBD *in vivo*." Although the IFN-gamma secretion that occurs in a mixed lymphocyte reaction is the result of histoincompatibility between two cell types, a

discovery that an antibody added to the *in vitro* cell culture reduces or suppresses the mixed lymphocyte reaction indicates that the antibody can be used to inhibit an immune response. Neither of the references cited by the Examiner (in the final paragraph on page 3 of the Office Action) suggests that an antibody that inhibits a mixed lymphocyte reaction *in vitro* would not be reasonably expected to inhibit an immune response *in vivo*. In addition, and as detailed in the preceding paragraph, the working examples contained in the specification as filed extend well beyond the disclosure of the results of a mixed lymphocyte reaction and demonstrate that a soluble KIM-1 protein is effective in an *in vivo* model of inflammatory bowel disease. The person of ordinary skill in the art having read the inventor's experimental results in treating a mouse model of inflammatory bowel disease would have reasonably expected that an antagonist anti-KIM-1 antibody would (like the KIM-1-Ig fusion protein) be effective in the treatment of inflammatory bowel disease as well as the other immunological disorders recited in the claims.

In view of the foregoing remarks, applicant respectfully submits that the person of ordinary skill in the art, at the time the present application was filed, would have been able to practice the claimed methods without undue experimentation and with a reasonable expectation of success. As a result, applicant requests that the Examiner withdraw the rejection.

CONCLUSIONS

Applicant respectfully submits that all grounds for rejection have been overcome and that all claims are now in condition for allowance. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 13751-055US1.

Respectfully submitted,

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